Status of the Claims

Claims 33, 37-51, and 53-74 are currently pending in the present application. Claims 1-32, 34-36, and 52 have been canceled. Claims 33, 37, 41, and 48-51 have been amended, and new claims 53-74 directed to the same invention as claim 33 have been added. The amendments to the claims and the addition of new claims supply separate specific embodiments of the claimed invention, based on specific characteristics of the invention. Claims 33 and 53-74 are currently examined.

Although, claims 37-51 have been withdrawn from examination as being directed to a separate invention, claims 37, 41, and 48-51 have been amended to correct their dependency. Applicants point out that claims 37-51 are now dependent upon new claim 58. Claim 58 is a necessary process for these products; thus, claim 58 is a linking claim. Thus, once claim 58 is found allowable, the restriction requirement as to the linked invention must be withdrawn and any claims depending from or otherwise include all the limitations of the allowable linking claim must be examined (see MPEP 809.03).

Amendments to the Claims

New claims 53-74 and the amendments to claims 33, 37, 41, and 48-51 do not introduce prohibited new matter. Claim 37, 41, and 48-51, although withdrawn from examination, have been amended to correct their dependency, since claim 36 has been canceled. Support for the amendment to claims 33 and the addition of new claims 53-74 is summarized in the Table below.

Claims	Support
33	original claim 1; paragraph [0078]
53, 54	original claim 36
55-57	original claim 52
58, 59	original claim 36
60, 61	original claims 36 and 52

62, 63	claims 37, 41, and 51
64, 65	claim 38
66, 67	claim 42
68, 69	claim 43
70, 71	claim 44
72, 73	claim 45
74	Examples 1-5

Rejections of the Claims Under 35 U.S.C. § 112, Second Paragraph

A. Claims 36 and 52 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

Claims 36 and 52 have been canceled and replaced with new claims. The new claims do not state that the ". . . compositions is selected from the group consisting of particles . . . liposomes, . . .and oil-in-water emulsions." Thus, Applicants respectfully request withdrawal of the rejection.

Rejection of the Claims Under 35 U.S.C. § 102(b)

Claim 33 is rejected 35 U.S.C. § 102(b) as being anticipated by Watts *et al.*

As amended, claim 33 and its dependent claims as they stand are directed to a method of identifying an optimal range of zeta potential for a composition for targeting to an activated vascular site. Claim 33 includes the step of evaluating zeta potential of the composition for vascular endothelial cell uptake wherein the composition is associated with a cationic component that targets the composition to an activated vascular site. The cited reference does not teach identifying an optimal range of zeta potential for a composition for targeting an activated vascular site and does not provide the step of evaluating zeta potential of a composition for vascular endothelial cell uptake.

An activated vascular site and a mucosa are very distinct tissues. Unlike an activated vascular site, the mucosa is the inner layer of any epithelially lined hollow organ. The mucosa has a complex multilayered structure. As described in the specification, the term "activated vascular sites" refers to vascular endothelial sites exhibiting an activated phenotype. As is well known, the vascular endothelium is a single pavement layer of cells which line the luminal surface of the entire vascular system and regulate the transport of macromolecules and blood components from interstitium to lumen.

Moreover, the route for targeting agents to the mucosa is distinct from the route for targeting agents to an activated vascular site required by the claim. Since the mucosa is accessible, the mucosa can be targeted from the outside by nasal, vaginal, or rectal administration. An activated vascular site , on the other hand, can only be targeted intravenously.

Furthermore, although the cited reference discloses using nitroglycerin, which the Office Action alleges to act on activated vascular sites, nitroglycerin is not a cationic component that targets an activated vascular site. Thus, the cited reference does not anticipate the claimed invention. Accordingly, Applicants request withdrawal of the rejection.

Rejection of the Claims Under 35 U.S.C. § 103(a)

Claims 36 and 52 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Watts *et al.*

Claims 36 and 52 have been canceled and replaced with claims 58-74. The claimed invention is directed to modifying an agent so that it targets an activated vascular site. The claims as they stand are directed to a method of modifying an agent to enhance its efficacy comprising associating one or more cationic components with an agent to produce a composition having an optimal range of zeta potential for specific targeting to an activated vascular site. The claims include the limitation that the cationic components target the composition to the activated vascular site.

The cited reference, Watts *et al.*, does not teach modifying an agent to enhance its efficacy by associating the agent with one or more cationic components to produce a composition having an optimal range of zeta potential for specific targeting to an activated

vascular site. The cited reference discloses the use of cationic compounds for targeting the mucosa only.

Moreover, as discussed under the response to the rejection under § 102, "an activated vascular site" is different from the mucosa. Their structures are distinct. The route for targeting an agent to the mucosa is different from that for targeting an activated vascular site. Accordingly, a method of targeting an agent to the mucosa as disclosed by Watts *et al.* would not have rendered the claimed method obvious.

Further, the Office Action alleges that the cited reference renders the claimed invention obvious because nitroglycerin, disclosed by the reference, acts on an activated vascular site. The claims include the limitation that the cationic components target the composition to the activated target site. Nitroglycerin is not a cationic molecule. Moreover, if nitroglycerin acts on an activated vascular site, one would not have been motivated to modify it by associating it with a cationic component to enhance its efficiency for targeting to an activated vascular site.

Accordingly, the claims are not obvious over the cited reference.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
Morgan, Lewis & Bockius LLP

Sally P. Teng
Registration No. 45,397

Date: October 4, 2004
Morgan, Lewis & Bockius LLP
Customer No. **09629**

1111 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
Tel: 202-739-3000
Fax: 202-739-3001